Helical Configuration of Poly(iminomethylenes). Screw Sense of Polymers Derived from Optically Active Alkyl Isocyanides

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ABSTRACT: The synthesis of three poly(iminomethylenes), \( [RN=C<]_n \), from optically active isocyanides is described. The group R includes \((\beta)-\text{CH}_3 \), \(\text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_3 \), \((\beta)-\text{CH}_3 \text{CH}_2 \text{CH} \), and \((\beta)-\text{CH}_2 \text{CH} \). From viscosity data it is estimated that MW’s range from 20,000 to 70,000. The central chain of these polymers is a rigid helix. The optically active side chains induce a predominance of one helical screw sense. In the UV spectra of the polymers the \( n^-n^+ \) transition of the \( \text{N} = \text{C} \) chromophore of the helical main chain is present as a shoulder at 310 nm. In model compounds \( \text{RN} = \text{CH} \cdot \text{CH}_2 \text{H}_2 \) this transition lies at an approximately 50 nm lower wavelength. The \( n^-n^+ \) transition of the \( \text{N} = \text{C} \) group is responsible for the CD spectrum in the region from 240 to 380 nm. The CD reveals a contribution from the side chains as well as from the excess helix. A comparison with the CD spectrum of enantiomerically pure \((\beta)-\text{poly}(\text{tert-butyliminomethylene})\) proves the excess helix to be of \( M \) sense. This excess diminishes from approximately 62% in \( R = (\beta)-\text{CH}_3 \text{CH}_2 \text{CH} \) to 20% in \( R = (\beta)-\text{CH}_2 \text{CH} \). This sequence is in agreement with predictions based on the polymerization mechanism.

Poly(isocyanides), more properly called poly(iminomethylenes), are obtained by the polymerization of isocyanides with nickel(II) catalysts.

\[ n\text{RN} = \text{C} \xrightarrow{\text{Ni}(II)} (\text{RN} = \text{C})_n \]

These polymers show atropisomerism, that is, stereoisomerism due to restricted rotation about single bonds, and represent a rare case of this kind of isomerism in polymers. They have a helical configuration and consequently are chiral. Poly(tert-butyliminomethylene) has been completely resolved by column chromatography. The support consisted of glass beads coated with poly([S]-sec-butyliminomethylene]. The right-handed (\( P \)) helix could be assigned to the dextrorotatory enantiomer. The left-handed (\( M \)) one to the levorotatory enantiomer. 

This resolution of poly(tert-butyliminomethylene) into enantiomers shows that polymerization of a nonchiral isocyanide gives a racemic mixture of \( P \) and \( M \) screws. However, when the monomer is one enantiomer of a chiral isocyanide, its polymer will be a mixture of diastereoisomers, and \( P \) and \( M \) screws will not be formed in equivalent amounts.

In a previous paper we compared the optical rotation values of various chiral isocyanides with those of their corresponding polymers. This comparison strongly supported the hypothesis that optically active isocyanides do indeed polymerize screw sense selectively. The screw sense of the various polymers was tentatively deduced from the optical rotation values. From the polymerization mechanism, rules were derived by means of which the screw sense can be predicted when an optically active isocyanide is polymerized by nickel(II).

Optical rotation values have been used frequently to draw conclusions about conformations of polymer chains in solution. However, in the present system one should be cautious about doing this, because poly(iminomethylenes) are highly rigid rod polymers. The rigid environment in the system \( R^*\text{N} = \text{C} \) might considerably affect the conformation of \( R^* \) and thus its contribution to the optical rotation. Therefore, when going from monomer to polymer the change in the optical rotation value is not necessarily due to the conformation of the polymer main chain exclusively.

More reliable information can be expected from circular dichroism (CD) data. Many of the polymers which we synthesized earlier had chromophores in their side chains. These chromophores might interfere with the helically arranged \( \text{C} = \text{N} \) chromophores of the main chain. These polymers are therefore less suitable for CD spectral analysis. Poly(iminomethylenes) derived from optically active alkyl isocyanides do not have additional chromophores and are more appropriate for a CD study. One such polymer, poly(sec-butyliminomethylene), was synthesized earlier. Its CD spectrum could not be recorded because of its complete insolubility in organic solvents. Yet its screw sense could be derived from the resolution process of poly(tert-butyliminomethylene). In this paper we describe the synthesis of three additional poly(alkyliminomethylene) prepared from optically active alkyl isocyanides, compounds 4a–c of Scheme I. These polymers are soluble in apolar organic solvents. Their CD spectra are compared with the spectrum of poly(tert-butyliminomethylene) (4d) and spectra of model compounds.

Results and Discussion

Synthesis. For the synthesis of polymers 4a–c as well as for their model compounds 5a–c one requires optically active amines as starting materials (Scheme I). 2-Octanamine (1a) was resolved through fractional crystallization of its bitartrate from water. After 12 crystallizations \(^1\text{H} NMR\) shift experiments showed that 1a was optically pure with \([\alpha]_D^{25} = 6.92°\). The absolute configuration of this enantiomer has been established to be \( R,11 (R)-3\)-Methyl-2-butanamine (1b) and \((R)-4\)-methyl-2-pentanamine (1c) were prepared from the amino acids L-valine and L-leucine, respectively, as outlined in Scheme II. The carboxylic function of the latter compounds was esterified and subsequently reduced to the hydroxymethyl group with \( \text{LiAlH}_4 \). We found it convenient to attach a benzoyl group to the \( \text{NH}_2 \) group of 6, as this facilitates the isolation of alcohol 9 from the reaction mixture. This benzoyl group is converted into a benzyl group during the reduction process. The latter group was removed by hydrogenolysis with palladium-on-charcoal. The unprotected alcohol 10 was treated with \( \text{HBr} \) in acetic acid to give 11. In this reaction a small amount of bromine was added as a catalyst. The bromide 11 was subjected to hydrogenolysis in an aqueous
sodium acetate-acetic acid buffer with palladium-on-carbon as catalyst. After workup the desired amines were isolated as their HCl salts. It follows from Scheme II that, when we start from the L-amino acids, the absolute configuration of the amines corresponds to these viscosities we determined a Mark–Houwink relation. To this end a sample of racemic 2-isocyanooctane was prepared as indicated for the optically active compound 3a. This racemic monomer was polymerized by nickel chloride under various conditions to give polymers having intrinsic viscosities \( [\eta] \) varying from 0.05 to 0.45 dL/g (toluene, 30.00 °C). Their weight-average molecular weights were determined by light scattering and were found to vary from 65,000 to 140,000. The ratio of \( M_w/M_n \) (gel permeation chromatography) for these polymers was about 6. From these data on the unfractionated samples the Mark–Houwink equation \( [\eta] = 1.4 \times 10^6 M_w^{1.75} \) was derived. Applying this equation to our optically active polymers 4a and 4c, we estimate that their viscosity-average molecular weights range from 20,000 to 70,000.

Compounds 4a–c showed a distinct N=C stretching vibration in the infrared spectrum at about 1630 cm\(^{-1}\). The UV spectra in hexane solution revealed a weak shoulder at about 310 nm (\( \epsilon \approx 60 \text{ L/(mol*cm)} \)) due to the \( n-\pi^* \) transition of the N=C chromophore. This shoulder is at the onset of a much stronger absorption band which has its maximum in the far-UV region. The CD spectra of the polymers were recorded in hexane and are presented in Figure 1. The optical rotation values are given in Table I.

As low molecular weight model compounds for our polymers the \( N \)-neopentylidene derivatives of amines 1, compounds 5, were synthesized. These compounds were selected because they can easily be prepared from piv-aldehyde and 1.17,18 Moreover, with these imines the problem of aldol-type condensation is avoided because an

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**Table I**

<table>
<thead>
<tr>
<th>( R )</th>
<th>( [M]^{[\alpha]}_{D} ) /deg</th>
</tr>
</thead>
<tbody>
<tr>
<td>a ((R)-n-C_6H_{13}CH(CH_3))</td>
<td>-66.3 34.5 47.3</td>
</tr>
<tr>
<td>b ((R)-(CH_3)_2CHCH(CH_3))</td>
<td>-23.5 76.1 -16.2</td>
</tr>
<tr>
<td>c ((R)-(CH_3)_2CHCHCH(CH_3))</td>
<td>-68.8 58.2 68.9</td>
</tr>
<tr>
<td>d ((CH_3)_3C)</td>
<td>+46.6</td>
</tr>
</tbody>
</table>

* In chloroform; 3, 1.1–1.9; 4, 0.25–0.8; 5, 0.9–2.3.  
* Per repeating unit RN=–C.  
* Taken from ref 2, M helix.

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**Figure 1**. CD spectra of poly(alkyliminomethylenes) in hexane solution: (---) 4a; (---) 4b; (---) 4c; (---) 4d.
α-CH group, such as that in 12, is absent. Also the formation of tautomeric enamine is prevented with what was found earlier for poly(tert-butyliminomethylene).  

Figure 1 shows that the maximum $\Delta \epsilon$ value of the positive CD band at 320-340 nm varies for the three polymers. If we assume that the main-chain helical configuration (apart from the $M$ or $P$ sense) is highly similar in polymers 4a-c, this $\Delta \epsilon$ value is a measure of the $M$-screw excess. We have calculated this excess from the maximum $\Delta \epsilon$ values, taking the $\Delta \epsilon$ of completely resolved poly(tert-butyliminomethylene) as the calibration value (Table III). Actually, for an accurate calculation the contributions made by the helical main chain and the chiral side chain should be considered separately. However, this is not really possible since the latter contribution is difficult to quantify for two reasons: (a) the lower wavelength region of the CD spectrum is disturbed by the effects of high-energy transitions and (b) the conformation of the side chain is unknown. This conformation is not necessarily similar to that in compounds 5, because both systems have a different steric environment. Therefore, the side-chain contribution cannot simply be taken from the model compounds. We have made the approximation that the $\Delta \epsilon$ values at longer wavelength are exclusively determined by the couplet. Thus, the numbers of Table III should be considered as useful only within the present series of polymers. They are probably lower limits.

The data in Table III show that the excess of $M$ screws diminishes with decreasing bulkiness of $R'$, as expressed by the $\lambda$ steric constant or approximately the Taft steric parameter. The $P$ excess in the polymer of $(R)$-sec-butyl isocyanide ($R' = C_3H_7$), which we synthesized earlier, fits into this series. We will try to explain this result in terms of the polymerization mechanism.

It was suggested earlier that polymerization of isocyanides by nickel(II) chloride proceeds via a circular sequence of insertion reactions around the nickel center (“merry-go-round” mechanism). The reaction starts from the square-planar complex Ni(CNR)$_4^{2+}$. In this complex, $\pi$ back-bonding from nickel to the isocyanide ligands is very small. The terminal carbon atom of such a ligand is

### Table II

<table>
<thead>
<tr>
<th>compd</th>
<th>$\lambda_{\text{max}}$/nm</th>
<th>$\epsilon/(L/\text{mol-cm})$</th>
<th>$\Delta \epsilon_{\text{max}}/(L/\text{mol-cm})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>248</td>
<td>86</td>
<td>-0.71</td>
</tr>
<tr>
<td>5b</td>
<td>249</td>
<td>86</td>
<td>-0.98</td>
</tr>
<tr>
<td>5c</td>
<td>248</td>
<td>88</td>
<td>-0.91</td>
</tr>
</tbody>
</table>

$^a$ Spectra were recorded in n-hexane solutions at 25°C.

### Table III

<table>
<thead>
<tr>
<th>$R'$</th>
<th>$\Delta \epsilon_{\text{max}}^{a}$ (L/(mol-cm))</th>
<th>$\Delta[M]^{b}$ deg</th>
<th>screw sense, % ee$^c$</th>
<th>$\lambda R'^d$</th>
<th>$-(E_0)_{\text{Taft}}^e$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_3H_7$</td>
<td>0.040</td>
<td>81.8</td>
<td>$P$</td>
<td>1.05</td>
<td>0.07</td>
</tr>
<tr>
<td>$n-C_3H_7$</td>
<td>0.115</td>
<td>127.1</td>
<td>$M$</td>
<td>1.1</td>
<td>0.30</td>
</tr>
<tr>
<td>$i-C_3H_7$</td>
<td>0.125</td>
<td>59.9</td>
<td>$M$</td>
<td>1.20</td>
<td>0.93</td>
</tr>
<tr>
<td>$i-C_2H_6$</td>
<td>0.20</td>
<td>46</td>
<td>$M$</td>
<td>1.27</td>
<td>0.47</td>
</tr>
<tr>
<td>$(t-C_3H_7NC)_n$</td>
<td>0.20</td>
<td>46</td>
<td>$M$</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ $\Delta \epsilon_{\text{max}}$ of positive band at 300-400 nm.  
$^b$ Difference between the molar optical rotation value of polymer 4 and that of model compound 5.  
$^c$ ee = enantiomeric excess of indicated screw, assuming complete stereoregular polymerization.  
$^d$ See ref 25.  
$^e$ Taft steric constant.  
$^f$ See ref 26.  

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easily attacked by a nucleophile X⁻ (e.g., Cl⁻) giving rise to ion 13 (Scheme III). In 13 the carbanion C⁻—N—C is attached coordinatively to the nickel center. Its plane is approximately perpendicular to the C⁻—C—C plane for steric reasons. There is free rotation around the bonds from Ni to C₁, C₂, and C₃, but not around that to C⁴. Carbon atom C₁ has gained in nucleophilicity. As a nucleophile it is able to attack a neighboring isocyanide carbon. This attack is facilitated when a new ligand enters apically from above and coordinates to the nickel. The direction of attack determines the screw sense. Continuing the sequence C¹ → C₂ → C₃ in a merry-go-round fashion, a right-handed helix is obtained. In a similar way the sequence C¹ → C₂ → C₃ results in a left-handed helix.

In our earlier studies we assumed that the group SMLC in 13 (the relative steric requirements of the substituents are denoted by small (S), medium (M), and large (L)) is predominantly in the Z position. In 13 the carbanion "C₁ plane for steric reasons. There is free rotation around the bonds from Ni to C₁, C₂, and C₃, but not around that to C⁴. Carbon atom C₁ has gained in nucleophilicity. As a nucleophile it is able to attack a neighboring isocyanide carbon. This attack is facilitated when a new ligand enters apically from above and coordinates to the nickel. The direction of attack determines the screw sense. Continuing the sequence C¹ → C₂ → C₃ in a merry-go-round fashion, a right-handed helix is obtained. In a similar way the sequence C¹ → C₂ → C₃ results in a left-handed helix.

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the synthesis of 1b. (R)-3-Methyl-2-butynamine (1b). An amount of 19 g (77 mmol) of 1b was subjected to catalytic reduction with 1 g of 10% palladium-on-carbon in a solution of 15 mL of acetic acid and 20 g of sodium acetate in 100 mL of water. After stirring for 4 h at room temperature and 1 atm of H₂ pressure, the calculated amount of H₂ was consumed. Subsequently, the catalyst was removed by filtration. The filtrate was rendered alkaline with an excess of NaOH and extracted with ether. After drying over 2H₂O; [H] NMR (CDCl₃) δ 1.65 (m, 3 H, CH₃), 1.00 (d, 3 H, CH₃), 0.90 (d, 6 H, (CH₂)₃C). (R)-N-Formyl-3-methyl-2-butynamine (2b). Amine 1b was liberated from its HCl salt with an excess of aqueous NaOH and neutralized with an excess of NaOH and extracted with ether. After drying over 2H₂O; [H] NMR (CDCl₃) δ 1.5-2.0 (m, 16 H, remaining H's). Compound 5d: bp 72 °C (60 mm); [α]₂[3] -50.3° (c 2.1, hexane) and [α]²[3] -49.0° (c 0.9, chloroform); IR (neat) 1668 (N=C) cm⁻¹; ¹H NMR (CDCl₃) δ 7.41 (1 H, =CH), 2.68 (1 H, CH₃), 1.6 (1 m, 1 H, CH), 1.05 (3 H, t-C₃H₇), 1.03 (3 H, CH₃), 0.77 and 0.85 (2d, 6 H, (CH₂)₃C). Acknowledgment. This research was supported by The Netherlands Foundation for Chemical Research (SON) with financial aid from The Netherlands Organization for the Advancement of Pure Research (ZWO). We thank Mr. H. Bokhorst for measuring the molecular weights.

References and Notes

(1) Part 14 in the series “Poly(aminomethylenes)”. For part 13 see ref. 2.


(9) For instance, see: Pino, P.; Salvadori, P.; Chiellini, E.; Luisi, P. L. Pure Appl. Chem. 1968, 16, 469.


(12) This procedure is generally applicable to the synthesis of optically active amino alcohols from the corresponding amino acids. Yields over 90% are normally obtained. Beijnen, A. J. M. van; Eijk, J. M. van der, unpublished results.


(14) Ugi, I.; Meyr, R. Angew. Chem. 1958, 70, 702.


(20) Reference 19, p 181.


Optically Active Polyampholytes Derived from L- and D-Carbylalanyl-L-histidine¹,²

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ABSTRACT: Two optically active polymers with the general structure \( \{\text{C=NCH(CH}_2\text{Im}]} \) were prepared by the polymerization of L- and D-carbylalanyl-L-histidine with catalytic amounts of nickel(II) chloride. The monomers were synthesized from the dipeptides L- and D-alamyl-L-histidine by converting the amino group of these compounds into an isocyano function. The polymer from D-alamyl-L-histidine has a \( \text{pK}_a(\text{ImH}^+) \) of 8.4. It shows a polyelectrolyte viscosity behavior. Its molar rotation is \( [\eta]^{30}_{578} \approx 0^\circ \). Its CD spectrum has a couplet indicative of a right-handed helix. The other polymer has a \( \text{pK}_a(\text{ImH}^+) \) of 9.4 and a nonpolyelectrolyte viscosity behavior. Its \( [\eta]^{30}_{578} \approx +1025^\circ \). The CD spectrum contains a single positive band, which does not provide information about the screw sense.

Enzymes combine high catalytic activity with high selectivity. Certain polymeric model systems, called synthenzymes, have equal or even greater activity. Striking examples are the ethylenimine-based systems developed by Klotz et al. and very recently by Kunitake et al. The success in this field contrasts sharply with the little progress that has been made in imitating the enantioselectivity of enzymes. In our opinion there is a lack of suitable chiral polymers which can be tested as enantioselective catalysts. We are currently investigating whether poly(isocyanides), more properly called poly(iminomethylenes), \( \{\text{R N =C}_n\} \), are useful as such polymers. These compounds are attractive for two reasons. First, they are readily obtainable from the monomeric isocyanides, \( \text{R N =C}_n \), with nickel chloride or a nickel(II) complex as catalyst. These monomers in turn can be prepared in great variety from the corresponding amines. Second, poly(iminomethylenes) have a stable helical structure. Left-handed and right-handed helices of poly(tert-butyliminomethylene) have been separated by resolution. Preferential formation of one screw occurs in the polymerization of one enantiomer of a chiral monomer.²

In previous papers we reported on the synthesis and catalytic activity of imidazole-containing poly(iminomethylenes) such as poly(carbylalanylhistidine), I, which could be models for hydrolytic enzymes. We were unable to get I in optically active form because its carboxyl- and imidazole-protected monomer suffered from a rapid racemization. This was due to the presence of both a basic imidazole function in the molecule and two electron-withdrawing substituents at the chiral center, viz., the isocyanate and carboxyl ester function.

We have now found that racemization problems can be avoided if one starts from isocyanides of dipeptides of histidine and other amino acids. The synthesis and physical properties of two polymers derived from such isocyanides, viz., poly(L-carbylalanyl-L-histidine) and poly(D-carbylalanyl-L-histidine), are described in this paper. Their catalytic activity in the hydrolysis of chiral esters will be described elsewhere.

Results and Discussion

Synthesis. As far as we are aware, isocyanides derived from dipeptides containing histidine have not been described in the literature. We have synthesized protected L- and D-carbylalanyl-L-histidine, compounds 6a and 6b, according to Scheme 1.

Prior to the coupling of the amino acids, the carboxyl group of histidine and the amino group of alanine were protected as the methyl ester and the formamide group, respectively. The latter protecting group was chosen because it can be transformed directly into an isocyanate function. Dicyclohexylcarbodiimide in acetonitrile/N,N-dimethylformamide was used as coupling agent. From the synthesis of I we learned that it is necessary to protect the imidazole nucleus before converting the N-formyl function into an isocyanate group. We chose the p-toluensulfonyl (Tos) group as an imidazole protecting group in 4. This group is easily introduced and can be removed under mild conditions, as we found recently. Moreover, a p-toluensulfonyl group lowers the basicity of the imidazole nucleus, which reduces the chance of